# Aflatoxins
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## Carcinogenicity

There is sufficient evidence for the carcinogenicity of aflatoxins in experimental animals (IARC V.10, 1976; IARC S.4, 1982; IARC S.7, 1987). Since the early report that contaminated peanut meal induced hepatomas in rats, many studies have demonstrated the carcinogenic potential of aflatoxins for the liver of rats. These compounds have been tested for carcinogenicity with many animal species by several routes of administration and found to produce tumors primarily of the liver, colon, and kidneys. When administered in the diet, aflatoxins induced hepatocellular carcinomas, carcinomas of the glandular stomach, mucinous adenocarcinomas of the colon, and kidney tumors in rats. Aflatoxins by the same route of administration induced hepatocellular carcinomas in Rhesus monkeys, a marmoset, and tree shrews. When administered in the diet, aflatoxin induced cholangiocellular carcinomas in hamsters. When administered by a single intragastric injection, the compound induced neoplastic hepatic nodules in rats. When administered by intraperitoneal injection to pregnant rats, aflatoxin induced liver and other tumors in the mothers and in their progeny. When administered orally or by intraperitoneal injection, aflatoxin induced pulmonary adenomas in mice. When administered by subcutaneous injection, aflatoxin induced sarcomas in mice and rats. Aflatoxins $G_1$ and $B_2$ are less potent hepatocarcinogens than is aflatoxin $B_1$ for rats dosed orally, but $G_1$ can induce a significant incidence of kidney tumors.

An IARC Working Group reported that there is sufficient evidence for the carcinogenicity of aflatoxins in humans (IARC S.7, 1987). A positive correlation between estimated aflatoxin intake or level of aflatoxin contamination of market food samples and cooked food and incidence of hepatocellular cancer was observed in early studies in Uganda, Swaziland, Thailand, and Kenya. Similar correlations between aflatoxin intake and hepatocellular cancer incidence and mortality have been reported from Mozambique and China. Studies conducted in different regions of Africa and Asia, where hepatocellular cancer incidence or mortality and aflatoxin intake were measured, revealed a highly significant correlation between these variables. In the southeast United States, in an area with a high average daily intake of aflatoxin, a 10% excess in hepatocellular cancer incidence was observed compared with areas with low aflatoxin intake. A case-control study in the Philippines, where mean aflatoxin contamination levels in dietary items were established and individual levels of aflatoxin consumption were determined retrospectively, demonstrated an increased, dose-related risk of developing hepatocellular cancer in persons with higher ingestion of aflatoxin. One major difficulty in interpreting these studies is potential confounding due to hepatitis virus B infection, which is endemic in many areas where the relationship between aflatoxin intake and hepatocellular carcinoma has been examined. However, in three recent studies, both factors have been taken into account. In China, both dietary and urinary levels of aflatoxins were found to be related to hepatocellular cancer incidence. Serological surveys did not show corresponding differences in the prevalence of the hepatitis B virus-carrier state. In Swaziland, in a study based on surveys of levels of aflatoxin intake across four broad geographic regions, liver cancer incidence was associated strongly with estimated levels of aflatoxin. In a multivariate analysis involving ten smaller subregions, aflatoxin exposure emerged as a more important determinant of the variation in liver cancer incidence than the prevalence of hepatitis B infection.

## Properties

Aflatoxins are toxic metabolites produced by certain types of fungi. They are intensely fluorescent in ultraviolet light and slightly soluble in water. When heated to decomposition, aflatoxins emit acrid smoke and irritating fumes.

## Use

Aflatoxins are used solely for research purposes. They are naturally occurring contaminants formed by specific fungi on food and agricultural products during conditions of high temperature and high humidity (IARC V.10, 1976).

## Production

Aflatoxins are not manufactured in commercial quantities. Total annual production usually does not exceed 0.25 lb (IARC V.10, 1976). Aflatoxins are produced by various strains of fungi in liquid fermentations or on solid food substrates. Aflatoxins occur mainly as contaminants on food and animal feed products; aflatoxin $B_1$ is the most frequent contaminant (IARC V.10, 1976). Aflatoxins were not included in the 1979 TSCA Inventory.

## Exposure

The primary route of potential human exposure to aflatoxins is ingestion of contaminated food. Grains, peanuts, tree nuts, and cottonseed meal are among the foods on which aflatoxin-producing fungi commonly grow. Meat, eggs, milk, and other edible products from animals that consume aflatoxin-contaminated feed are additional sources of potential exposure. Americans may consume up to an estimated 0.15-0.50 μg of aflatoxins daily (IARC V.10, 1976).

## Regulations

EPA regulates aflatoxins under the Resource Conservation and Recovery Act (RCRA), which designates aflatoxins as hazardous constituents of waste. Additionally, EPA's Carcinogen Assessment Group considers aflatoxins to be potentially carcinogenic. FDA, under the Federal Food, Drug and Cosmetic Act and the Public Service Act, have regulated any materials or ingredients that could be contaminated with aflatoxins. OSHA regulates aflatoxins under the Hazard Communication Standard and as a chemical hazard in laboratories.